Characterization of high-affinity peptides and their feasibility for use in nanotherapeutics targeting leukemia stem cells.

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Public Summary:
This article described a small molecule that can specifically bind to leukemia stem cells (LSC), a special subgroup of leukemia cells that are resistant to chemotherapy, and can regenerate leukemia cells to cause leukemia recurrence. This small molecule can potentially target and kill LSC. A nanoparticle drug delivery system was also developed. These nanoparticles are loaded with chemotherapeutic drug inside, and decorated with the LSC-targeting molecule on the surface. The resulting nanoparticles can work like "smart missiles" to seek and kill LSC after intravenous injection.

Scientific Abstract:
Peptides featuring the LR(S/T) motif were identified that could specifically bind to the C-type lectin-like molecule-1 (CLL1), a protein preferentially expressed on acute myeloid leukemia stem cells (LSCs). Micellar nanoparticles were covalently decorated with CLL1-targeting peptides for targeted drug delivery. The resulting peptide-coated nanoparticles were 13.5 nm in diameter and could be loaded with 5 mg of daunorubicin per 20 mg of telodendrimers. These "targeting nanomicelles" transported the drug load to the interior of cells expressing CLL1 and to LSCs isolated from clinical specimens in vitro, but did not bind to normal blood or normal hematopoietic stem cells. The presence of CLL1-targeting peptides on the surface of the nanomicelles enabled the improved binding and delivery of substantially more daunorubicin into the cells expressing CLL1 and CD34(+) leukemic cells compared with unmodified nanomicelles. In conclusion, nanomicelles coated with CLL1-targeting peptides are potentially useful for eradicating LSCs and improving leukemia therapy.